Invasive Infection with Multidrug-Resistant *Salmonella enterica* Serotype Typhimurium Definitive Type 104 among HIV-Infected Adults

Tamara L. Fisk,[1] Brita E. Lundberg,[1] Jodie L. Guest,[2] Susan Ray,[1,4] Timothy J. Barrett,[3] Ben Holland,[3] Karen Stamey,[3] Frederick J. Angulo,[3] and Monica M. Farley[1,2,4]

[1]Department of Medicine, Division of Infectious Diseases, Emory University, [2]The Veterans Affairs Medical Center, [3]Division of Bacterial and Mycotic Disease, National Center for Infectious Disease, Centers for Disease Control and Prevention, and [4]Georgia Emerging Infections Program, Atlanta, Georgia

Background. Multidrug-resistant *Salmonella enterica* serotype Typhimurium definitive type 104 (MRDT104), with resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (R-type ACSSuT), was first detected in the United States in 1985 [1], and the prevalence increased to account for nearly 7% of *Salmonella* infections in 1998 [2].

Methods. A retrospective study of *S.* Typhimurium infections in an urban health care system assessed whether infection with an antibiotic-resistant strain—and specifically MRDT104—was associated with invasive disease or HIV infection. Sixty cases of *S.* Typhimurium infection were identified.

Results. Of the 50 isolates available for analysis, 30 (60%) were MRDT104. Pathogens were isolated from blood in 25 (83%) of 30 patients infected with MRDT104, compared with 10 (50%) of 20 patients who were infected with non-MRDT104 strains ($P = .01$). Among isolates obtained from 32 HIV-infected patients, 19 (95%) of 20 MRDT104 isolates were from blood specimens, compared with 8 (66%) of 12 non-MRDT104 isolates ($P = .05$).

Conclusions. MRDT104 accounted for the majority of *S.* Typhimurium infections in this patient population, and MRDT104 infections were more invasive than non-MRDT104 infections, particularly in HIV-infected persons.

Each year, an estimated 1.4 million persons are infected with *Salmonella* in the United States [3]. Most infections result in mild-to-moderate gastroenteritis, but severe infections can occur, resulting in bacteremia, meningitis, and death. *Salmonella* infections lead to an estimated 16,430 hospitalizations and 582 deaths annually [3]. From 1996 through 1999, an annual average of 35,099 culture-confirmed *Salmonella* infections were reported to the Centers for Disease Control and Prevention (CDC; Atlanta, GA) [2], of which 11,041 (58%) occurred in persons ⩾14 years of age (CDC; unpublished data). In the CDC's Foodborne Diseases Active Surveillance Network (FoodNet), an enhanced surveillance effort in several selected states (including Georgia), *Salmonella* serotypes were isolated from blood or CSF samples from 6.5% of persons ⩾14 years of age who had culture-confirmed *Salmonella* infection during 1996–1999 (FoodNet; unpublished data); 0.9% of persons ⩾14 years of age with culture-confirmed *Salmonella* infection died.

Salmonella enterica serotype Typhimurium was the most frequently identified serotype among culture-confirmed infections reported to the CDC during 1996–1999, accounting for 27% of the reported infections [4]. In recent years, antimicrobial resistance among *Salmonella* strains has become a concern, particularly among *S.* Typhimurium strains [5]. National surveillance for antimicrobial resistance among *Salmonella* strains in the United States is conducted through the National Antimicrobial Resistance Monitoring System for Enteric Bacteria [6]. Multidrug-resistant *S.* Typhimurium definitive type 104 (MRDT104), with resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (R-type ACSSuT), was first detected in the United States in 1985

Received 18 July 2004; accepted 8 November 2004; electronically published 24 February 2005.

Reprints or correspondence: Dr. Brita E. Lundberg (brita.lundberg@medscape.com).

Clinical Infectious Diseases 2005; 40:1016–21

1058-4838/2005/4007-0017$15.00

[1] and has emerged as the most common multidrug-resistant strain of *Salmonella* in the United States and several other countries in the mid-1990s [7, 8]. In 1998, 28% of *S.* Typhimurium isolates were ACSSuT; of these isolates, 86% were definitive type 104 [2]. Therefore, 7% of human *Salmonella* infections in the United States in 1998 were due to MRDT104 [2].

Outbreaks of MRDT104 infection in the United States have been associated with exposure to cattle [9] and consumption of dairy products [10]. Prior use of antimicrobial agents for treatment of another illness has also been associated with sporadic MRDT104 infection [11]. MRDT104 infection has been reported to be associated with increased severity of infection, including an increased case-fatality rate in the United Kingdom [12]. In studies in the United States and Denmark, MRDT104 infection has also been associated with increased rates of hospitalization and increased mortality [13, 14].

HIV-infected persons represent a patient population at increased risk for invasive, recurrent, and—most notably—drug-resistant *Salmonella* infections [15–19]. Neither the association between HIV infection and subsequent MRDT104 infection nor the clinical consequences of MRDT104 infection among HIV-infected persons has, to our knowledge, been previously reported. A retrospective review of *S.* Typhimurium infections in 60 consecutive adult patients at an urban medical center was conducted to determine whether infection with antibiotic-resistant strains—specifically, MRDT104—was associated with invasive disease and whether HIV infection was associated with infection due to MRDT104, compared with infection due to other *S.* Typhimurium strains.

MATERIALS AND METHODS

This study was conducted at the Grady Memorial Hospital (GMH) and its affiliated clinics. GMH is an 850-bed municipal hospital in Atlanta.

Study population. Cases of infection with *S.* Typhimurium were identified by reviewing the surveillance registry of cases collected by the Georgia FoodNet site, a program that has conducted a population-based active surveillance for laboratory-confirmed *Salmonella* infections since 1 October 1995. All adults (defined as persons $\geqslant$14 years old) with culture-confirmed *S.* Typhimurium isolated at the GMH laboratory during a 51-month period (October 1995–December 1999) were included in the study; the cutoff age of 14 years was selected to include those adults most likely to be sexually active and therefore at risk for HIV infection. If *S.* Typhimurium was isolated from >1 specimen (i.e., isolated from both blood and stool samples) from a single patient, only the blood isolate was considered in the analysis. If isolates from the same site were obtained on >1 occasion from the same patient, only the initial isolate was considered.

Medical record review. A review was conducted of patients' medical, pharmacy, and laboratory records. Data abstracted from patients' medical charts included the source(s) of specimen(s) that yielded *S.* Typhimurium, use of antimicrobial agents in the month before isolation of *S.* Typhimurium, treatment course, and patient outcome. Computerized laboratory records were also reviewed for the results of serological tests for HIV and, among HIV-infected patients, $CD4^+$ cell counts (as determined by flow cytometry) and HIV RNA load (as determined by RT-PCR). HIV infection was considered to be confirmed if there was a documented ELISA result positive for HIV that was confirmed by Western blot; patients with an ELISA result negative for HIV within 1 year after infection with *S.* Typhimurium were considered to be HIV uninfected. For patients without an HIV test result, an 18-month follow-up of patient records and the confidential HIV registry maintained by the GMH laboratory (which covers all affiliated outpatient clinics and the hospital) was conducted for a later diagnosis of HIV infection. For the purposes of analysis, patients without HIV test results were considered to be uninfected with HIV. Inpatient and outpatient computerized pharmacy records and hospital records were reviewed to determine history of use of antimicrobial agents. Recurrence of any *Salmonella* infection was defined as a subsequent isolation of *S.* Typhimurium after completion of a prescribed course of antibiotics as an inpatient or outpatient after initial isolation of *S.* Typhimurium. Deaths within 21 days after specimen collection were included in case-fatality calculations.

Microbiological analysis. All stool and blood specimens that were submitted to the GMH laboratory were cultured for *Salmonella* using standard methods [20]. Isolates were initially cultured on xylose-lactose-deoxycholate and Hektoen-enteric agar and an enriched broth media (selenite; Carr-Scarborough). After incubation, typical colonies were picked and subcultured to the Rollender and Beckford tube system (Remel) for identification. *Salmonella* isolates were serotyped at the Georgia State Public Health Laboratory according to the Kauffman and White scheme [21, 22]. *Salmonella* isolates identified at GMH laboratory from December 1995 through December 1999 were stored at $-70°C$ before microbiological analysis.

Expanded antimicrobial resistance testing was performed at the CDC with use of the Sensititre broth microdilution system (Trek Diagnostics). At the CDC, partial range MICs of 14 antimicrobial agents were determined according to NCCLS standards. These antimicrobial agents included ampicillin, tetracycline, trimethoprim-sulfamethoxazole, ciprofloxacin, amikacin, amoxicillin/clavulanic acid, cephalothin, chloramphenicol, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, and ceftriaxone. Resistance was determined according to NCCLS interpretive standards.

Salmonella isolates were phage typed at the CDC according to the international phage typing system [23]. Isolates classified as definitive type (DT) 104, DT104a, DT104b, or U302 are considered to be closely related and are categorized as DT104 complex; they will be referred to hereafter as "DT104 isolates." Isolates other than DT104 isolates include those that react to phages but do not conform to a specific phage type (commonly referred to as Reaction Does Not Conform [RDNC] isolates) and untypable isolates. In this analysis, DT104 isolates with resistance to ⩾5 antimicrobial agents are defined as MRDT104.

PFGE analysis was conducted at the Emory University Division of Infectious Diseases Laboratory (Atlanta) and the Georgia State Public Health Laboratory (Atlanta) using the standardized laboratory protocol for molecular subtyping of foodborne bacterial pathogens by PFGE [24]. Gel images were compared using the Dice coefficient and the unweighted pair group method with Molecular Analyst Fingerprinting Plus software for Windows, version 1.0 (BioRad Laboratories), at the CDC. The Tenover criteria for relatedness were used; isolates with ⩽3-band difference were considered to have the same PFGE pattern [25].

Data analysis. Fisher's exact test or the χ^2 test was used to compare categorical variables; P values <.05 were considered to be statistically significant. Nonnormally distributed continuous variables were compared using the Wilcoxon rank sum test. Data analysis was performed using EpiInfo software, version 6.04 (CDC).

RESULTS

During the 51 months of the study period, the GMH laboratory identified 275 culture-confirmed *Salmonella* cases. Of the isolates associated with these cases, 105 (38%) were from adults (i.e., persons ⩾14 years of age). Of these, 104 were serotyped, and 60 (58%) were *S.* Typhimurium. The proportion of *Salmonella* isolates that were *S.* Typhimurium was 3 (75%) of 4 in 1995, 16 (55%) of 29 in 1996, 12 (44%) of 27 in 1997, 14 (64%) of 22 in 1998, and 15 (68%) of 22 in 1999.

Clinical factors and HIV infection. Of the 60 adults with culture-confirmed *S.* Typhimurium infection, 46 (77%) were hospitalized, 4 in the intensive care unit. *S.* Typhimurium was isolated from blood specimens in 44 (73%) of the patients, stool specimens in 13 (22%) of the patients, urine specimens in 3 (5%) of the patients, and both blood and stool specimens in 4 (6%) of the patients. HIV testing was conducted for 45 of the 60 patients; 39 patients (65%) had confirmed HIV infection. HIV testing was not conducted for 15 patients; 18-month follow-up of these patients' medical records found that none of these patients had later received a diagnosis of HIV infection. Five (8%) of the 60 patients had a recurrent *S.* Typhimurium infection. Eleven patients (18%) died within 21 days of specimen collection. None of the 60 patients had a recorded recent history of exposure to livestock or international travel. Fifteen (25%) patients received antimicrobial agents in the month before onset of *Salmonella* infection.

The relationship between HIV infection and demographic and clinical parameters for the 60 patients with *S.* Typhimurium infection is shown in table 1. $CD4^+$ cell counts were determined for 35 of 39 HIV-infected patients with *S.* Typhimurium infection within 3 months before illness onset; $CD4^+$ cell counts ranged from 1 to 416 cells/μL (median $CD4^+$ cell count, 57 cells/μL). Viral loads, which were available for 16 HIV-infected patients with *S.* Typhimurium infection in the 3 months before illness onset, ranged from 31,180 to >750,000 copies/mL.

$CD4^+$ cell count correlated with outcome. The 4 patients with $CD4^+$ cell counts who died (median $CD4^+$ cell count, 39 cells/μL) had lower median $CD4^+$ cell counts than did the 31 patients who survived (median $CD4^+$ cell count, 96 cells/μL; $P = .02$). Similarly, among the 31 HIV-infected patients with *S.* Typhimurium infection who had a $CD4^+$ cell count determined and survived, the 5 patients who developed recurrent infection had lower median $CD4^+$ cell counts (median $CD4^+$ cell count, 9 cells/μL) than did the 26 patients without recurrence (median $CD4^+$ cell count, 96 cells/μL; $P = .2$).

Microbiologic analysis. Isolates were available for microbiological analysis for 50 (83%) of 60 patients with *S.* Typhimurium infection. The 50 patients for whom isolates were available did not differ significantly from the 10 patients for whom isolates were not available in terms of the rate of hospitalization, bacteremia, HIV infection, or death (data not shown).

Of the 50 available *S.* Typhimurium isolates, 36 (72%) of the isolates were resistant to ampicillin, 36 (72%) to streptomycin, 36 (72%) to sulfamethoxazole, 35 (70%) to tetracycline, 32 (64%) to chloramphenicol, 4 (8%) to kanamycin, 1 (2%) to gentamicin, and 1 (2%) to trimethoprim. Twelve (24%) of

Table 1. Demographic and clinical characteristics of adults presenting with *Salmonella enterica* serotype Typhimurium infection at Grady Memorial Hospital, October 1995–December 1999, by HIV infection status.

Variable	HIV-infected patients (n = 39)	HIV-uninfected patients (n = 21)	P
Male sex	33 (85)	11 (52)	.008
Age, mean years (range)	40 (24–54)	52 (16–90)	.008
Bacteremia present	34 (87)	10 (48)	.001
Received antibiotics ⩽1 month before hospitalization	13 (39)	2 (10)	.04
Infection recurred	5 (13)	0 (0)	.15
Hospitalized	32 (82)	14 (66)	.21
Duration of hospitalization, median days (range)	6.5 (1–50)	7.7 (1–30)	.11
Died	6 (15)	5 (24)	.73

NOTE. Data are no. (%) of patients, unless otherwise indicated.

the isolates were pansusceptible; 1 isolate (2%) was resistant to 1 antimicrobial agent, 2 (4%) to 2 antimicrobial agents, none to 3 antimicrobial agents, 2 (4%) to 4 antimicrobial agents, 30 (60%) to 5 antimicrobial agents, and 3 (6%) to 6 antimicrobial agents; therefore, 33 (66%) of these isolates were resistant to $\geqslant$5 antimicrobial agents. R-type ACSSuT was seen in 29 isolates; R-type ACSSuT with additional resistance to kanamycin (R-type ACKSSuT) was seen in 2 isolates; R-type ACSSuT with additional resistance to trimethoprim (R-type ACSSuTTm) was seen in 1 isolate; and resistance to ampicillin, kanamycin, streptomycin, sulfamethoxazole, and tetracycline (R-type AKSSuT) was seen in 1 isolate. All isolates retained susceptibility to quinolones and extended-spectrum cephalosporins.

Phage typing and PFGE of isolates. All 50 available *S.* Typhimurium isolates were phage typed and subtyped by PFGE (table 2). Thirty-four (68%) of the isolates belonged to the DT104 complex; 22 were DT104a, 5 were DT104b, 4 were DT104, and 3 were U302. Of the 34 DT104 complex isolates, 2 were pansusceptible, 28 were R-type ACSSuT, and 1 isolate each was R-type ACSSuTTm, R-type ACKSSuT, R-type ASSuT, and resistant to ampicillin and sulfamethoxazole (R-type ASu). Therefore, 30 (60%) of the 50 *S.* Typhimurium isolates were MRDT104. All 50 isolates were subtyped by PFGE. Four PFGE patterns (A, C, D, and E) were shared by >1 isolate. These 4 patterns accounted for 41 (82%) of the 50 isolates. Thirty-one isolates (62%) were pattern A. All 31 pattern A isolates belonged to the DT104 complex; 29 (96%) of 30 MRDT104 isolates were pattern A.

The proportion of *S.* Typhimurium isolates that were MRDT104 for each year during the 5-year study period was 2 (100%) of 2 in 1995, 5 (50%) of 10 in 1996, 5 (44%) of 11 in 1997, 7 (58%) of 12 in 1998, and 11 (73%) of 15 in 1999.

Bacteremia. Of the 50 *S.* Typhimurium isolates, 35 (70%) were isolated from blood specimens. Patients with *S.* Typhimurium MRDT104 isolates were more likely than other patients to be bacteremic; the isolates obtained from 25 (83%) of 30 patients with MRDT104 infections were from blood specimens, compared with 10 (50%) of 20 non-MRDT104 isolates ($P = .01$). Seven (58%) of 12 pansusceptible isolates were from blood specimens, and 28 (73%) of 38 *S.* Typhimurium isolates with resistance to >1 antibiotic were from blood specimens ($P = .47$).

MRDT104 and HIV infection. Thirty-two (64%) of 50 patients with available isolates were HIV infected. Twenty (67%) of 30 patients with *S.* Typhimurium MRDT104 isolates were HIV infected, compared with 12 (60%) of 20 patients with non-MRDT104 *Salmonella* ($P = .63$). Nine (75%) of 12 patients with pansusceptible infections were HIV infected. Among isolates obtained from the 32 HIV-infected patients, 19 (95%) of 20 MRDT104 isolates were from blood specimens, compared with 8 (66%) of 12 other isolates ($P = .05$). Among isolates obtained from the 18 HIV-uninfected patients, 6 (60%) of 10 MRDT104 isolates were from blood specimens, compared with 2 (25%) of 8 other isolates ($P = .3$; stratified $P = .01$).

Table 2. Phage type, PFGE pattern, and antibiotic susceptibilities of 50 *Salmonella enterica* serotype Typhimurium isolates, October 1995 through December 1999.

PFGE pattern, phage type	No. of isolates	Antibiotic susceptibility pattern (no. of isolates)
DT104 patterns		
A		
DT104	3	**ACSSuT** (2), **ACSSuTTm** (1)
DT104a	21	**ACSSuT** (18), **ACKSSuT** (1), ASu (1), ASSuT (1)
DT104b	4	**ACSSuT** (4)
U302	3	**ACSSuT** (3)
B		
DT104	1	**ACSSuT** (1)
C		
DT104a	1	Pansusceptible (1)
DT104b	1	Pansusceptible (1)
Non-DT104 patterns		
D		
DT1	1	Pansusceptible (1)
DT126	2	Pansusceptible (2)
RDNC	2	Pansusceptible (2)
E		
Untypable	3	ACKSSuT (1), AKSSuT (1), AKSSu (1)
Unique patterns		
DT1	1	Pansusceptible (1)
DT126	1	GS (1)
RDNC	3	Pansusceptible (3)
Untypable	3	ACSSuT (1), T (1), pansusceptible (1)

NOTE. Multidrug-resistant DT104 isolates appear in boldface. A, ampicillin resistance; C, chloramphenicol resistance; G, gentamicin resistance; K, kanamycin resistance; RDNC, isolates that react to phages but do not conform to a specific phage type; S, streptomycin resistance; Su, sulfamethoxazole resistance; T, tetracycline resistance; Tm, trimethoprim-sulfamethoxazole resistance.

Outcomes. Of the 50 patients with available *S.* Typhimurium isolates, 37 (74%) were hospitalized. The hospitalization rates were similar among patients with isolates of various phenotypes: 25 (83%) of 30 patients with *S.* Typhimurium MRDT104 isolates were hospitalized, compared with 12 (60%) of 20 with other isolates ($P = .4$). Eight (67%) of 12 patients with pansusceptible isolates were hospitalized. Hospitalization rates were similar even when the data for hospitalization were stratified by bloodstream infection (data not shown). Of the 4 patients requiring admission to the intensive care unit, 3 (75%) of 4 had MRDT104 isolates.

Death due to *Salmonella* occurred in 8 (16%) of 50 patients with available isolates: 5 (17%) of 30 patients with MRDT104 died, compared with 3 (15%) of 20 with other infections ($P = .59$). Two (17%) of 12 patients with pansusceptible infections died.

Of the 5 patients who developed recurrent infection, all were HIV-infected, and 4 were infected with MRDT104. All 5 patients appeared to experience relapse with the same organism that caused the initial infection, because PFGE patterns and antibiotic susceptibilities of isolates from initial and recurrent episodes were identical except for the development of intermediate susceptibility to amoxicillin-clavulanate (MIC, 16 μg/mL) and resistance to cephalothin in 1 patient with 4 recurrences of infection.

Prior antibiotic treatment. Of the 50 patients with available isolates, 11 (22%) received an antimicrobial agent in the month before illness onset. Patients with MRDT104 (4 [13%] of 30) were not more likely to receive an antimicrobial agent before illness onset than were patients with pansusceptible isolates (3 [25%] of 12; $P = .8$). The person with a trimethoprim-resistant isolate (R-type ACSSuTTm) was HIV-infected and had received trimethoprim-sulfamethoxazole for *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*) pneumonia prophylaxis in the month before illness onset.

DISCUSSION

To our knowledge, this is the first report to evaluate *S.* Typhimurium drug resistance and its association with clinical parameters in a population with relatively high rates of HIV infection. We observed that *S.* Typhimurium MRDT104 caused a high proportion (35%) of cases of salmonellosis in our population; 58% of *Salmonella* isolates were *S.* Typhimurium, and 60% of these were MRDT104. In contrast, in national surveillance conducted in 1998, an estimated 7% of *Salmonella* isolates were MRDT104 [2]. Among patients infected with *S.* Typhimurium, MRDT104 infections were more likely to be invasive than were non-MRDT104 *S.* Typhimurium infections, particularly in HIV-infected persons.

A higher prevalence of *Salmonella* infections and increased rates of bacteremia and relapse have been noted previously in HIV-infected persons, leading to the inclusion of *Salmonella* septicemia as an AIDS-indicator disease [16–18]. Although MRDT104 isolates were not more common among HIV-infected patients with *S.* Typhimurium than they were among patients with *S.* Typhimurium who were not infected with HIV, MRDT104 strains were more likely than other *S.* Typhimurium strains to be isolated from blood specimens, with the overall effect largely attributed to increased invasiveness in HIV-infected persons. Among HIV-infected persons in our study, 19 (95%) of 20 MRDT104 isolates were from blood specimens, compared with 8 (66%) of 12 non-MRDT104 isolates ($P = .05$).

Despite decreased invasiveness of MRDT104 in animal models [26], several clinical studies have found increased mortality and evidence of increased morbidity among patients with drug-resistant *S.* Typhimurium infection [12–15]. One case-control study showed increased rates of hospital admission and a 10-fold increase in the mortality rate associated with DT104 infection, compared with infection with other *Salmonella* strains [12]. Our study, however, did not find increased mortality associated with DT104 infection, despite detecting increased invasiveness associated with MRDT104 infection (although overall mortality was higher than the national rates associated with *S.* Typhimurium infection). All recurrences of infection in our study occurred among HIV-infected persons. On the basis of the results of PFGE and antibiotic susceptibility testing, it was determined that these represented relapses rather than new infections. An increased risk of relapse and death correlated with low $CD4^+$ cell counts.

The high prevalence of MRDT104 among *S.* Typhimurium isolates in this study contributed to the fact that a high proportion of isolates (70%) were obtained from blood specimens. In contrast, in national surveillance data from 1999, only 4% of *S.* Typhimurium isolates were from blood specimens (CDC; unpublished data). The discrepancy between the rates of bacteremia found in this study and those in the national surveillance data may be due, in part, to the setting of our study: a large municipal health care system, in which patients tend to present later in the course of illness.

Prior use of antibiotics has been reported to be a risk factor for multidrug-resistant *Salmonella* infection, including infection due to MRDT104 [11, 27]. In this study, prior use of antibiotics by patients was common: one-fourth of all case patients and one-third of HIV-infected patients received antibiotics either as prophylaxis or for treatment of other processes before illness onset. However, among patients with *S.* Typhimurium infection, prior use of antibiotics was not a risk factor for infection with multidrug-resistant *S.* Typhimurium. Although multidrug resistance was common among *S.* Typhimurium isolates in this study, all isolates retained susceptibility to quinolones and extended spectrum cephalosporins, the most common treatment choices in adults and children, respectively.

In our study, we found that infection due to *S.* Typhimurium MRDT104 was more invasive than infection due to other *S.* Typhimurium strains, particularly in HIV-infected persons. The high rate of infection with MRDT104 *S.* Typhimurium in this population and the apparent increase in the invasiveness of these infections may lead to increased morbidity and health care costs. Additional studies are required to determine the epidemiological risk factors and molecular basis for the increased invasiveness of MRDT104 observed in this patient population.

Acknowledgments

We thank Suzanne Segler and Shama Desai, for assistance in *Salmonella* case identification from the EIP database; the staffs at the CDC microbiology laboratory and the Emory University Infectious Disease clinical research laboratories, for excellent technical assistance; Annalyn Brondyke, for secretarial assistance; and William J. Burman and C. Robert Horsburgh, Jr., for a critical reading of the manuscript.

Potential conflicts of interest. All authors: no conflicts.

References

1. Ribot E, Wierzba R, Angulo F, Barrett T. *Salmonella enterica* serotype Typhimurium DT104 Isolated from Humans, United States, 1985, 1990, and 1995. Emerg Infect Dis **2002**; 8:387–91.
2. Rabatsky-Ehr T, Whichard J, Rossiter S, et al. Multidrug-resistant strains of *Salmonella enterica* Typhimurium, United States, 1997–1998. Emerg Infect Dis **2004**; 10:795–801.
3. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. Emerg Infect Dis **1999**; 5:607–21.
4. Centers for Disease Control and Prevention (CDC). Salmonella Surveillance: Annual Summary, 2000. Atlanta, GA: US Department of Health and Human Services, CDC, **2000**.
5. Angulo F, Johnson K, Tauxe R, Cohen M. Origins and consequences of antimicrobial-resistant nontyphoidal *Salmonella:* implications for the use of fluoroquinolones in food animals. Microbial Drug Resistance **2000**; 6:77–83.
6. Marano N, Rossiter S, Stamey K, et al. The National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria, 1996–1999: surveillance for action. JAVMA **2000**; 217:1829–30.
7. Glynn MK, Bopp C, Dewitt W, Dabney P, Mokhtar M, Angulo FJ. Emergence of multidrug-resistant *Salmonella enterica* serotype typhimurium DT 104 infections in the United States. N Engl J Med **1998**;338: 1333–8.
8. Threlfall EJ, Frost JA, Ward LR, Rowe B. Increasing spectrum of resistance in multiresistant *Salmonella typhimurium.* Lancet **1996**; 347: 1053–4.
9. Friedman C, Brady R, Celotti M, et al. An outbreak of multi-drug resistant *Salmonella* serotype Typhimurium definitive type 104 (DT104) infections in humans and cattle in Vermont [abstract 15]. In: Program and abstracts of the International Conference on Emerging Infectious Diseases (Atlanta, GA). Washington, DC: American Society of Microbiology, **1998**.
10. Villar RJ, Macek MC, Simons S, et al. Investigation of multidrug-resistant *Salmonella* serotype typhimurium DT 104 infecttions linked to raw-milk cheese in Washington state. JAMA **1999**; 281:1811–6.
11. Glynn MK, Reddy V, Hutwagner L, et al. Prior antimicrobial agent use increases sporadic infections with multidrug-resistant *Salmonella enterica* serotype Typhimurium: a FoodNet case-control study, 1997–1997. Clin Infect Dis **2004**; 38(Suppl 3):S227–36.
12. Wall PG, Morgan D, Ryan M, et al. A case control study of infection with an epidemic strain of multi-resistant *Salmonella typhimurium* DT104 in England and Wales. Commun Dis Rep CDR Rev **1994**; 4: R130–5.
13. Varma J, Molbak K, Angulo F. Antimicrobial-resistant non-typhoidal *Salmonella* is associated with excess bloodstream infections and hospitalizations. J Infect Dis **2005**; 191:554–61.
14. Helms M, Vastrup P, Gerner-Smidt P, Molbak K. Excess mortality associated with antimicrobial drug-resistant *Salmonella* Typhimurium. Emerg Infect Dis **2002**; 8:490–95.
15. Casin I, Breuil J, Brisabois A, Moury F, Grimont F, Collatz E. Multidrug-resistant human and animal *Salmonella typhimurium* isolates in France belong primarily to a DT104 clone with the chromosome- and integron-encoded beta-lactamase PSE-1. J Infect Dis **1999**; 179: 1173–82.
16. Fischl MA, Dickinson GM, Sinave C, Pitchenik AE, Cleary TJ. *Salmonella* bacteremia as manifestation of acquired immunodeficiency syndrome. Arch Intern Med **1986**; 146:113–5.
17. Levine WC, Buehler JW, Bean NH, Tauxe RV. Epidemiology of non-typhoidal *Salmonella* bacteremia during the human immunodeficiency virus epidemic. J Infect Dis **1991**; 164:81–7.
18. Sperber SJ, Schleupner CJ. Salmonellosis during infection with human immunodeficiency virus. Rev Infect Dis **1987**; 9:925–34.
19. Wolday D, Erge W. Antimicrobial sensitivity pattern of *Salmonella:* comparison of isolates from HIV-infected and HIV-uninfected patients. Trop Doct **1998**; 28:139–41.
20. Farmer J, Kelly M. Enterobacteriaceae. In: Balows A, Hausler WJ, eds. Manual of clinical microbiology. 5th ed. Washington, DC: American Society for Microbiology, **1991**:371–3.
21. Popoff M, Le Minor L. Antigenic formulas of the *Salmonella* serovars. 7th revision. Paris, France: Pasteur Institute, **1997**.
22. Popoff M, Bockemuhl J, Brenner F. Supplement 1998 (no. 42) to the Kauffman-White scheme. Res Microbiol **2000**; 151:63–5.
23. Anderson ES, Ward LR, De Saxe MJ, de Sa JD. Bacteriophage-typing designations of *Salmonella typhimurium.* J Hyg (London) **1977**; 78: 297–300.
24. Gautom RK. Rapid pulsed-field gel electrophoresis protocol for typing of *Escherichia coli* O157:H7 and other gram-negative organisms in 1 day. J Clin Microbiol **1997**; 35:2977–80.
25. Tenover F, Arbeit R, Goering R, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol **1995**; 33:2233–9.
26. Carlson SA, Browning M, Ferris KE, Jones BD. Identification of diminished tissue culture invasiveness among multiple antibiotic resistant *Salmonella typhimurium* DT104. Microb Pathog **2000**; 28:37–44.
27. Lee L, Puhr N, Maloney K, Bean N, Tauxe R. Increase in antimicrobial-resistant *Salmonella* infections in the United States, 1989–1990. J Infect Dis **1994**; 170:128–34.